REMARKS

The claims have been amended to simplify the issues. The possibility of "an immunologically effective portion thereof" has been deleted and the claims have thus been limited to human prostate-specific membrane antigen (PSMA) or prostatic acid phosphatase (PAP). PSA is no longer in the claims because only an immunologically reactive portion thereof was included previously. Claims to eliciting an antitumor immune response using full-length PSA have already been issued in U.S. patent 5,925,362. Claims 14 and 17 have been canceled as no longer relevant.

The Invention

In view of the rejection under 35 U.S.C. § 103 on page 10 of the Office action, applicants believe that perhaps the nature of the invention requires further explanation. The antitumor response is elicited according to the method of the invention, not in response to a tumor-associated antigen - a concept well understood in the prior art. On the contrary, the antitumor immune response is elicited with regard to an antigen normally present in the prostate. The invention takes advantage of the fact that the prostate is not an essential organ and thus an immune response which could include disruption of normal tissue is acceptable. See page 4, lines 11-22. No prior art document suggests this approach to treatment of tumors.

Rejection of Claims 13 and 17-24 Under 35 U.S.C. § 112, first paragraph (Written Description)

It is believed that the amendment to the claims and the following explanation are completely responsive to this objection. The claims have now been limited to PSMA and PAP and nucleotide sequences encoding them *per se*. The structure of these proteins and of the nucleic acids encoding them is known in the art. See page 8 of the specification, lines 1-5 (PAP) and page 9 of the specification, lines 9-11 (PSMA). Thus, it is clear that a written description of the active ingredients is included in the specification by reference to the knowledge of the art. It is assumed that the Office is not requesting reproduction of the sequence from these published articles in the body of the specification, any more than the Office would require the applicant to include the structure of aspirin or lovastatin in methods of treatment involving these drugs.

Applicants note, with appreciation, that claims 14-17 are not included in this rejection. Perhaps it was not apparent that previous claim 13 referred only to PSA, PSMA and PAP. In any event, in light of the foregoing comments, it is believed that the rejection for lack of written description may be withdrawn.

The Rejection of Claims 13-24 Under 35 U.S.C. § 112, first paragraph (Lack of Enablement)

It is believed that the amendment to this claim disposes of this rejection as the Office acknowledges that the specification is enabling for full-length PSA, PSMA and PAP.

The Rejection of Claim 24 Under 35 U.S.C. § 112, first paragraph

The subject matter of claim 24 represents subject matter originally claimed in the application as filed (claim 12). Original claim 12 required that the subject be

(a) afflicted with metastatic prostate cancer; and/or

(b) been surgically treated to excise the tumor but is at risk for recurrence (with the optional limitation that the subject is in a "neoadjuvant" setting) or

(c) wherein the subject is a potential prostate tumor-bearing subject.

The changes simply delete the last alternative (c) and the optional limitation to the second (b). Thus, the subject matter is completely disclosed *in haec verba* in the application as originally filed. Accordingly, this basis for rejection may properly be withdrawn.

The Rejection of Claims 13-24 as Asserted Obvious Over Spitler in Combination With Israeli

This basis for rejection is somewhat astounding in view of the view taken in the context of the § 112 rejections concerning the unpredictability of the vaccine art. The infamous "squeeze" appears to be at play here. Nevertheless, there is a different reason that the invention method is not rendered obvious by the cited documents. The primary reference, Spitler, refers to the use of a tumor associated antigen which is not found in normal tissue as the active ingredient in a vaccine. The whole concept of the invention resides in using instead of such an obvious target, an antigen that occurs in normal tissue. This is nowhere suggested in the cited art. The

citation of Israeli is also somewhat astounding in view of the assertion that the application lacks written description for PSMA.

In any event, the asserted motivation for combining the documents ignores the fact that PSMA is not a tumor-associated antigen not associated with normal tissue. Thus, the disclosure of Spitler where an antigen uniquely associated with the tumor and not expressed in normal tissue and thus foreign to the host is used as an active ingredient in a vaccine provides no incentive (absent the invention) to combine its teachings with a document which teaches a normally produced antigen. For this reason, the rejection over Spitler in combination with Israeli may properly be withdrawn.

CONCLUSION

The claims have been limited to full-length forms of PSMA and PAP. These are well known antigens whose genes have been cloned and are available in the art. Accordingly, the written description requirement is clearly met; enablement has been acknowledged by the Office and applicants are appreciative of this. The cited art fails to suggest the central concept of the invention, which is the use of a normally produced antigen as an active ingredient in an antitumor vaccine. Accordingly, it is respectfully submitted that claims 13, 15-16 and 18-24, all pending claims, are in a position for allowance and passage of these claims to issue is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket No. 204372000301. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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By: Kate H. Murashige

Kate H. Murashige
Registration No. 29,959

Morrison & Foerster LLP
3811 Valley Centre Drive
Suite 500
San Diego, California 92130-2332
Telephone: (858) 720-7962
Facsimile: (858) 720-5125

EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

13. (Thrice amended) A method to elicit an antitumor immune response to prostate tumors in a subject, which method comprises

administering to said subject at least one active ingredient formulated for administration to said subject,

wherein said active ingredient comprises or expresses at least one antigen over-represented in the prostate gland [or an immunologically effective portion thereof],

wherein said [antigen] active ingredient is [an immunologically reactive portion of human prostate-specific antigen (PSA); or]

human prostate-specific membrane antigen (PSMA) [or an immunologically effective portion thereof]; or

[human prostate-specific membrane antigen (PSMA) or an immunologically effective portion thereof; or]

prostatic acid phosphatase (PAP) [or an immunologically reactive portion thereof]; or mixtures of the foregoing; or

[wherein said active ingredient comprises] is a nucleic acid that generates said antigen or antigens *in situ*.